REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Streptococcus pneumoniae is an important cause of otitis media, meningitis, bacteremia and pneumonia, and a leading cause of fatal infections in the elderly and persons with underlying medical conditions, such as pulmonary disease, liver disease, alcoholism, sickle cell anemia, cerebrospinal fluid leaks, acquired immune deficiency syndrome (AIDS), and in patients undergoing immunosuppressive therapy. It is also a leading cause of morbidity in young children. Pneumococcal infections cause approximately 40,000 deaths in the U.S. yearly. The most severe pneumococcal infections involve invasive meningitis and bacteremia infections, of which there are 3,000 and 50,000 cases annually, respectively.

Despite the use of antibiotics and vaccines, the prevalence of pneumococcal infections has declined little over the last twenty-five years; the case-fatality rate for bacteremia is reported to be 15-20% in the general population, 30-40% in the elderly, and 36% in inner-city African Americans. Less severe forms of pneumococcal disease are pneumonia, of which there are 500,000 cases annually in the U.S., and otitis media in children, of which there are an estimated 7,000,000 cases annually in the U.S. caused by pneumococcus. Strains of drug-resistant *S. pneumoniae* are becoming ever more common in the U.S. and worldwide. In some areas, as many as 30% of pneumococcal isolates are resistant to penicillin. The increase in antimicrobial resistant pneumococcus further emphasizes the need for preventing pneumococcal infections.

Pneumococcus asymptomatically colonizes the upper respiratory tract of normal individuals; disease often results from the spread of organisms from the nasopharynx to other tissues during opportunistic events. The incidence of carriage in humans varies with age and circumstances. Carrier rates in children are typically higher than those of adults. Studies have demonstrated that 38 to 60% of preschool children, 29 to 35% of grammar school children and 9 to 25% of junior high school children are carriers of pneumococcus. Among adults, the rate of carriage drops to 6% for those without children at home, and to 18 to 29% for those with children at home. It is not surprising that the higher rate of carriage in children than in adults parallels the incidence of pneumococcal disease in these populations.

An attractive goal for streptococcal vaccination is to reduce carriage in the vaccinated populations and subsequently reduce the incidence of pneumococcal disease. There is speculation that a reduction in pneumococcal carriage rates by vaccination could reduce the incidence of the disease in non-vaccinated individuals as well as in vaccinated individuals. This "herd immunity" induced by vaccination against upper respiratory bacterial pathogens has been observed using the *Haemophilus influenzae* type b conjugate vaccines.

It is generally accepted that immunity to *S. pneumoniae* can be mediated by specific antibodies against the polysaccharide capsule of the pneumococcus. However, neonates and young children fail to make an adequate immune response against most capsular polysaccharide antigens and can have repeated infections involving the same capsular serotype. One approach to immunizing infants against a number of encapsulated bacteria is to conjugate the capsular polysaccharide antigens to protein to make them immunogenic. This approach has been successful, for example, with *H. influenzae b.*

However, there are over ninety known capsular serotypes of *S. pneumoniae*, of which twenty-three account for about 95% of the disease. For a pneumococcal polysaccharide-protein conjugate to be successful, the capsular types responsible for most pneumococcal infections would have to be made adequately immunogenic. This approach may be difficult, because the twenty-three polysaccharides included in the presently-available vaccine are not all adequately immunogenic, even in adults.

Protection mediated by anti-capsular polysaccharide antibody responses are restricted to the polysaccharide type. Different polysaccharide types differentially facilitate virulence in humans and other species. Pneumococcal vaccines have been developed by combining 23 different capsular polysaccharides that are the prevalent types of human pneumococcal disease. These 23 polysaccharide types have been used in a licensed pneumococcal vaccine since 1983. The licensed 23-valent polysaccharide vaccine has a reported efficacy of approximately 60% in preventing bacteremia caused pneumococci in healthy adults.

However, the efficacy of the vaccine has been controversial, and at times, the justification for the recommended use of the vaccine questioned. It has been speculated that the efficacy of this vaccine is negatively affected by having to combine 23 different antigens. Having a large number of antigens combined in a single formulation may negatively affect the antibody responses to individual types within this mixture because of antigenic

competition. The efficacy is also affected by the fact that the 23 serotypes encompass all serological types associated with human infections and carriage.

An alternative approach to protecting against pneumococcal infection, especially for protecting children, and also the elderly, would be to identify protein antigens that could elicit protective immune responses. Such proteins may serve as a vaccine by themselves, may be used in conjunction with successful polysaccharide-protein conjugates, or as carriers for polysaccharides.

Pneumococcal Surface Protein A or PspA has been identified as an antigen; and, its DNA and amino acid sequences have been investigated. PspA is useful in eliciting protective immune responses. PspA or fragments thereof can be used in immunological, immunogenic or vaccine compositions; and, such compositions can contain different types of PspAs or fragments from different types of PspAs. Further, such compositions can be administered by injection, or mucosally or orally, or by means of a vector expressing the PspA or fragment thereof.

Studies on PspA led to the discovery of a PspA-like protein and a *pspA*-like gene, now termed PspC and *pspC*. Indeed, early patent literature termed PspC as "PspA-like".

It is believed that heretofore that epitopic regions of PspC have not been disclosed or suggested. It is likewise believed that heretofore different clades of PspC have not been taught or suggested. Further, it is believed that heretofore DNA encoding epitopic regions of PspC have not been disclosed or suggested. Further still, it is believed that heretofore immunological, immunogenic or vaccine compositions comprising at least one PspC and/or portions thereof (such as at least one epitopic region of at least one PspC and/or at least one polypeptide encoding at least one epitope of at least one PspC), either alone or in further combination with at least one second pneumococcal antigen, such as at least one different PspC and/or a fragment thereof and/or at least one PspA and/or at least one epitopic region of at least one PspA and/or at least one polypeptide comprising at least one epitope of PspA, have not been taught or suggested.

Alternative vaccination strategies are desirable as such provide alternative immunological, immunogenic or vaccine compositions, as well as alternative routes to administration or alternative routes to responses. It would be advantageous to provide an immunological composition or vaccination regimen which elicits protection against various

diversified pneumococcal strains, without having to combine a large number of possibly competitive antigens within the same formulation. And, it is advantageous to provide additional antigens and epitopes for use in immunological, immunogenic and/or vaccine compositions, e.g., to provide alternative compositions containing or comprising such antigens or epitopes either alone or in combination with different antigens.

Furthermore it is advantageous to provide a better understanding of the pathogenic mechanisms of pneumococci, as this can lead to the development of improved vaccines, diagnoses and treatments.

The present invention is directed to achieving these objectives.

The rejection of claims 34, 42, and 43 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments.

The objection to the disclosure for containing an embedded hyperlink and/or other form of browser-executable code is obviated in view of the above amendments.

The rejection of claims 34, 42, and 43 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,573,082 to Choi et al. ("Choi"), U.S. Patent No. 6,503,511 to Wizemann et al. ("Wizemann"), or U.S. Patent No. 6,291,654 to Hostetter et al. ("Hostetter") is respectfully traversed.

Choi discloses antigenic polypeptides of *Streptococcus pneumoniae*. It is the position of the U.S. Patent and Trademark Office ("PTO") that the claimed polypeptide molecule of the present invention, i.e., amino acids 263-442 of SEQ ID NO: 13, is 100% identical to the SP023 polypeptide molecule (i.e., SEQ ID NO: 38) disclosed in Choi. Additionally, it is the PTO's position that the claimed polypeptide molecule of the present invention, i.e., SEQ ID NO: 13, is 54.1% identical to the SP023 polypeptide molecule (i.e., SEQ ID NO: 38) disclosed in Choi.

Wizemann relates to derivatives of choline binding proteins for vaccines. In particular, Wizemann discloses polypeptide molecules encoding *Streptococcus pneumoniae* choline binding proteins (CBPs). It is the PTO's position that the claimed polypeptide molecule of the present invention, i.e., amino acids 263-442 of SEQ ID NO: 13, is 100%, 99.4%, and 90.4% identical to the *S. pneumoniae* CBP-encoding polypeptide molecules (i.e., SEQ ID NOs: 9, 6, and 16, respectively) disclosed in Wizemann. Additionally, it is the PTO's position that the claimed polypeptide molecule of the present invention, i.e., SEQ ID

NO: 13, is 86.5%, 85.8%, and 55.4% identical to the *S. pneumoniae* CBP-encoding polypeptide molecules (i.e., SEQ ID NOs: 9, 6, and 16, respectively) disclosed in Wizemann.

Hostetter discloses a protein molecule encoding a C3 binding protein from *Streptococcus pneumoniae*. It is the PTO's position that the claimed polypeptide molecules of the present invention, i.e., SEQ ID NO: 13 and amino acids 263-442 of SEQ ID NO: 13, are 68.1% and 90.2% identical, respectively, to the *S. pneumoniae* C3 binding protein molecule (i.e., SEQ ID NO: 6) disclosed in Hostetter.

Since none of the cited references teaches the specific nucleic acid sequence of SEQ ID NO: 13, as recited in the amended claims, the rejection under 35 U.S.C. § 102(e) should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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